REMARKS

Claims 1-6, 8-10, 12-15, and 19-30 are pending in the application. Claim 7 has been cancelled. Claims 1-5, 9, 10, 12, and 15 have been amended. Claims 19-30 are new. Support for the amendments can be found in the original claims as well as throughout the specification. No new matter has been added.

Drawings

The drawings were objected to by the Examiner as indicated by the Draftsperson on PTO Form 948. The drawings have been edited to remove informalities as suggested by the Draftsperson and new formal drawings are being submitted herewith, thereby obviating this rejection.

Rejections under 35 U.S.C. § 101

Claims 1-4 and 15 are rejected under 35 U.S.C. § 101 as "it is PTO policy not to issue claims that encompass humans." The claims have been amended to recite non-human mammals, thereby obviating this rejection.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-4 are rejected under 35 U.S.C. § 112, first paragraph

> ...because the specification, while being enabling for a trangenic system for purification of a target polypeptide comprising a transgenic mammal, does not reasonably provide enablement for said system comprising any transgenic animal.

Specifically, the Examiner asserts "Only mammals produce milk...the specification fails to teach any other animals that can produce milk." The claims have been amended to recite a mammal, thereby obviating this rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-10 and 12-15 are rejected under 35 U.S.C. § 112, second paragraph "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

Specifically, the Examiner rejects claims 1-4 asserting that "the recitation of a 'transgenic system...' renders the claims indefinite because it is unclear whether Applicants are claiming a composition or a method." The claims, as amended, are directed to a system for purification of a target polypeptide having a bindable epitope. The system, as recited in the amended claims, clearly refers to a composition, a system made of at least three related elements: 1) a milk sample which includes a multivalent polypeptide that has a first binding moiety that binds the bindable epitope of the target polypeptide and a second binding moiety that binds a matrix; 2) a product which includes the target polypeptide having the bindable epitope, wherein the milk sample and the product form a reaction mixture; and 3) a matrix which binds the second binding moiety of the multivalent binding polypeptide. Together these make a "system." Thus, claims 1-4, as amended, are clearly written as composition claims. Therefore, Applicants respectfully request that this rejection be withdrawn.

The Examiner further asserts that "[r]egarding claim 3, the term 'binding moiety' renders the claim indefinite because it is unclear which binding moiety Applicants are referring to." Claim 3 has been amended to recite the first binding moiety, thereby obviating this rejection.

In addition, the Examiner rejects claim 4 asserting that "the term 'catalytic domain' renders the claim indefinite." Specifically, the Examiner asserts that "[a] 'catalytic domain' is the part of an enzyme that is responsible for enzymatic reaction. However, not every enzyme can remove the bindable epitope of the target polypeptide..." Applicants respectfully traverse this rejection. Claim 4 recites a catalytic domain which is "...capable of removing a bindable epitope of the target polypeptide". Thus, it is clear that not every enzyme is included. Only those enzymes capable of removing a bindable epitope are included. Moreover, Applicants clearly provide catalytic domains which include a protease activity (page 4, lines 8-19, page 8, lines 13-16, and page 19, lines 5-7), for example, chymosin and amidase as described in the

specification. The language of the claim is such that if an enzyme – such as the kinase or methylase – recited by the Examiner is not capable of removing a bindable epitope, it would not be covered by the claim. Therefore, Applicants respectfully request that this rejection be withdrawn.

Regarding claims 4-10 and 12-15, the Examiner rejects these claims asserting that "the term 'transgenic multivalent binding polypeptide' renders the claim indefinite because the nature of said polypeptide is unclear." According to the Examiner, "It is unclear whether the polypeptide is made *in vivo* by a transgenic animal or *in vitro* by a cell that normally does not express said polypeptide." Applicants respectfully traverse this rejection. The claims specifically recite a "transgenically produced" multivalent polypeptide, not a recombinantly produced polypeptide. Thus, the claims clearly limit the multivalent binding polypeptide to one that is transgenic. It is known in the art that this term does not refer to cell culture, and thus it is not indefinite. Therefore, Applicants respectfully request that this rejection be withdrawn.

Regarding claims 5-10 and 12-15, the Examiner states that "...the thereby... renders the claims indefinite because it is unclear what 'the thereby' means within the context of the sentence." The claims have been amended recite, "...to thereby...", thus obviating this rejection.

Regarding claims 9 and 10, the Examiner rejects these claims asserting that "the term 'a fragment thereof' renders the claims indefinite because it is unclear which part or size fragment of protein L or cellulose binding domain is referred to. The claims have been amended to recite a "functional fragment thereof." By requiring that the fragment be functional, it is clear that only those fragments capable of binding are covered. Specifically, the claims refer to fragments of protein L that are capable of binding the bindable epitope of the target polypeptide and fragments of cellulose binding domain that are capable of binding a matrix. Therefore, Applicants respectfully request that this rejection be withdrawn.

Regarding the rejection of claim 15, the Examiner asserts that while claim 15 "...recites the limitation 'another transgenic animal' in line 2..., the parent claim 12 does not recite any 'transgenic animal.' There is insufficient antecedent basis for this limitation in the claim." Claim 12 has been amended to recite "...a non-human transgenic mammal..." and claim 15 has been amended to recite "...another non-human transgenic mammal...", thereby obviating this rejection.

Regarding the rejection of claims 5-10 and 12-15, the Examiner states that these claims are "incomplete for omitting the steps." According to the Examiner, the "omitted steps are: eluting the target polypeptide from the matrix; [and,] removing the bindable epitope from said target polypeptide." The Applicants respectfully traverse this rejection. The steps that the Examiner wishes to add are not essential steps in the claims. The claims are directed to "obtaining a target polypeptide ... from a product...", e.g., milk. The steps recited by the Examiner are not necessary in obtaining a target polypeptide. The final steps of the instant claim, "contacting the reaction mixture..." and "removing reaction mixture..." suitably accomplish the necessary task in obtaining a target polypeptide from a product. It is not necessary to elute the polypeptide from the matrix nor is it necessary to remove the bindable epitope from the target polypeptide. By contacting with the matrix and removing unbound reaction mixture, the target polypeptide has already been obtained from the product. Therefore, Applicants respectfully request that this rejection be withdrawn.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be allowed. Enclosed is a $460 check for the Petition for Extension of Time fee and a $99 check for excess claims. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

Claim 7 has been cancelled.

Claims 19-30 have been added.

Claims 1, 2, 3, 4, 5, 9, 10, 12, and 15 have been amended as follows:

1. (Amended) A [transgenic] system for purification of a target polypeptide having a bindable epitope, the system comprising:

[a transgenic animal having in its genome a nucleic acid encoding] a milk sample comprising a multivalent binding polypeptide [under control of a promoter which directs expression in mammary epithelial cells], wherein the multivalent binding polypeptide comprises a first binding moiety which specifically binds the bindable epitope of the target polypeptide and a second binding moiety which specifically binds a matrix[, whereby such transgenic multivalent binding polypeptide is expressed at high levels in milk of the transgenic animal];

a product comprising the target polypeptide having the bindable epitope, wherein the milk sample and the product form a reaction mixture; and

a matrix to which the second binding moiety of the multivalent binding polypeptide specifically binds.

2. (Amended) The system according to claim 1, wherein the bindable epitope of the target polypeptide is [removable]capable of being removed.

3. (Amended) The system according to claim 2, wherein the first binding moiety of the multivalent binding polypeptide [removes]is capable of removing the bindable epitope.

4. (Amended) The system according to claim 2, wherein the system further comprises:

a second [transgenic]transgenically produced multivalent binding polypeptide comprising a first catalytic domain and a second binding moiety which specifically [binds]is capable of

binding a matrix, wherein the catalytic domain is capable of removing the bindable epitope of the target polypeptide; and

a second matrix which specifically [binds]is capable of binding the second binding moiety of the second [transgenic]transgenically produced multivalent binding polypeptide, wherein the matrix is different than the matrix specifically bound by the second binding moiety of the first transgenic multivalent binding polypeptide.

5. (Amended) A method of obtaining a target polypeptide having a bindable epitope from a product, the method comprising:

contacting a product which comprises a target polypeptide having a bindable epitope with a [transgenic]transgenically produced multivalent binding polypeptide, wherein the transgenically produced multivalent binding polypeptide comprises a first binding moiety which specifically binds the bindable epitope of the target polypeptide and a second binding moiety which specifically binds a matrix, to thereby provide a reaction mixture;

contacting the reaction mixture with a matrix which specifically binds the second binding moiety of the multivalent binding polypeptide; and

removing reaction mixture which does not bind to the matrix, to [the]thereby obtain the target polypeptide from the product.

[7. (Cancelled) The method according to claim 5, wherein the product is milk.]

9. (Amended) The method according to claim 8, wherein the first binding moiety of the transgenic multivalent binding polypeptide is protein L or a functional fragment thereof.

10. (Amended) The method according to claim 9, wherein the second binding moiety of the transgenic multivalent binding polypeptide is a cellulose bind domain (CBD) or a functional fragment thereof.

12. (Amended) A method of obtaining a target polypeptide having a bindable epitope from milk of a non-human transgenic mammal, the method comprising:

contacting milk which comprises a target polypeptide having a bindable epitope with a [transgenic]transgenically produced multivalent binding polypeptide, wherein the multivalent binding polypeptide comprises a first binding moiety which specifically binds the bindable epitope of the target polypeptide and a second binding moiety which specifically binds a matrix, to thereby provide a reaction mixture;

contacting the reaction mixture with a matrix which specifically binds the second binding moiety of the multivalent binding polypeptide; and

removing reaction mixture which does not bind to the matrix, to [the]thereby obtain the target polypeptide from the milk.

15. (Amended) The method according to claim 12, wherein the [transgenic]transgenically produced multivalent binding polypeptide is [present] produced in milk from another non-human transgenic mammal[animal].

19. (New) The system according to claim 2, wherein the transgenically produced multivalent polypeptide further comprises a third binding moiety and the third binding moiety is capable of removing the bindable epitope from the target polypeptide.

20. (New) The method according to claim 5, wherein the transgenically produced multivalent polypeptide further comprises a third binding moiety and the third binding moiety is capable of removing the bindable epitope from the target polypeptide.

21. (New) The method of claim 5, wherein the first binding moiety of the multivalent binding polypeptide is an antibody or functional fragment thereof which binds the bindable epitope of the target polypeptide.

22. (New) The method of claim 5, wherein the second binding moiety of the multivalent binding polypeptide is a cellulose binding domain (CBD), or a functional fragment thereof.

23. (New) The method of claim 5, wherein the target polypeptide is a receptor and the first binding moiety of the multivalent binding polypeptide is a ligand which binds the bindable epitope of the receptor.

24. (New) The method of claim 5, wherein the first binding moiety of the multivalent binding polypeptide is a receptor which binds the bindable epitope of the target polypeptide.

25. (New) The method according to claim 12, wherein the transgenically produced multivalent binding polypeptide is produced in the milk of the non-human transgenic mammal.

26. (New) The method of claim 12, wherein the transgenically produced multivalent polypeptide further comprises a third binding moiety and the third binding moiety is capable of removing the bindable epitope from the target polypeptide.

27. (New) The method of claim 12, wherein the first binding moiety of the multivalent binding polypeptide is an antibody or functional fragment thereof which binds the bindable epitope of the target polypeptide.

28. (New) The method of claim 12, wherein the second binding moiety of the multivalent binding polypeptide is a cellulose binding domain (CBD), or a functional fragment thereof.

29. (New) The method of claim 12, wherein the target polypeptide is a receptor and the first binding moiety of the multivalent binding polypeptide is a ligand which binds the bindable epitope of the receptor.

30. (New) The method of claim 12, wherein the first binding moiety of the multivalent binding polypeptide is a receptor which binds the bindable epitope of the target polypeptide.